European Review for Medical and Pharmacological Sciences 2021; 25: 1006-1015

Clinical pharmacist interventions in managing Key Monitoring Drugs in China

J. YANG[1,2], L. ZHENG[2], W.-G. YU[1], Y.-C. GU[1]

[1]School of Medicine and Pharmacy, Ocean University of China, Qingdao, Shandong, P.R. China
[2]Department of Pharmacy, Shandong Provincial Third Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, P.R. China

Jing Yang and Lei Zheng contributed equally to this work

Abstract. – OBJECTIVE: Drug-related problems (DRPs) are common in hospitalized patients receiving Key Monitoring Drugs. Clinical pharmacy services have the potential to minimize drug-related harm and improve patient care. The aim of this study is to standardize the clinical application of Key Monitoring Drugs and reduce drug-related problems (DRPs) and associated costs, using clinical pharmacist interventions.

PATIENTS AND METHODS: Clinical pharmacists formulate management measures for Key Monitoring Drugs using evidence-based medicine and analyze the DRPs of Key Monitoring Drugs in China at the Shandong Provincial Third Hospital over a period of five years, from 2015 to 2019.

RESULTS: In 2019, the total cost of the use of Key Monitoring Drugs decreased by 10.12 million CNY, in comparison with the cost in 2015. The proportion of revenue generated from Key Monitoring Drugs also decreased by 11.49% compared with 2015. In addition, the cost per capita of Key Monitoring Drugs has gradually decreased; this resulted in a saving of 580.07 CNY per capita in 2019 compared with 2015. Over this time, the DRPs associated with Key Monitoring Drugs decreased by 45.50%. Through administrative intervention, prescription review, information management, and pharmaco-economic evaluation, a scientific management system for Key Monitoring Drugs has been established over this time, which standardizes the use of Key Monitoring Drugs and reduces their associated costs.

CONCLUSIONS: Clinical pharmacists' interventions can assist in the early detection of drug-related problems associated with Key Monitoring Drugs and prevent any resulting harm to patients.

Key Words:
Key monitoring drugs, Drug cost, Evidence-based medicine, Clinical pharmacist, Drug-related problems.

Introduction

On 1st July 2019, the first edition of a national advisory concerning the applications of Key Monitoring Drugs was released by the Medical Administration Bureau of the National Health Commission of the People's Republic of China. Key Monitoring Drugs are defined, in three regards, as "drugs that help to increase the effect of the main therapeutic drugs or increase their efficacy by influencing the absorption, mechanism of action and metabolism of the main therapeutic drugs, or drugs that help to prevent and treat diseases or functional disorders"[1]. Key Monitoring Drugs included the following: drugs that enhance tissue metabolism; vitamins; electrolytes; drugs for enteral and parenteral nutrition; neurotrophic drugs; free radical scavenging drugs; traditional Chinese medicine for promoting blood circulation and removing stasis; and drugs for the auxiliary treatment of liver disease, tumors, and other conditions.

In recent years, with the development of new approaches to disease rejuvenation and with the onset of modern medical treatments, national medical expenses have increased year after year, of which drug expenses account for a large proportion. The use of Key Monitoring Drugs, in particular, has grown rapidly owing to their wide applications and the commercial promotion of these drugs. The rise in the clinical application of Key Monitoring Drugs has resulted in many drug-related problems, as has been determined through prescription analysis. The resulting problems have imposed a huge financial burden on patients and placed significant pressure on the medical insurance fund[2].

Corresponding Authors: Wen-Gong Yu, MD; e-mail: marcin.wengongyuouc@163.com
Yu-Chao Gu, MD; e-mail: guyuchao2021@163.com

Global healthcare systems are aimed at improving patients' safety by preventing drug-related problems (DRPs). Thereby, it is essential for such systems to promote the rational use of Key Monitoring Drugs, which will subsequently reduce their associated costs. In addition, there are many drugs that are closely related to one another, and it can be difficult for a doctor to select precisely the correct drug for a patient's treatment. One problem that must be addressed is the need for criteria on how scientific methods can be applied by doctors to make comprehensive evaluations of similar drugs to select the correct drug using scientific methods[3]. Since 2015, a preference has arisen for the scientific management of Key Monitoring Drugs based on evidence-based medicine, and some progress has been made toward this end. The aim of this study is to assess the outcomes of clinical pharmacological interventions in relation to the irrational use of Key Monitoring Drugs, as well as to construct a sustainable and improved model for the management of Key Monitoring Drugs.

Compared with previous decades, this study will demonstrate how clinical pharmacist-led services for the improvement of medication safety in hospitals and in the community can be shown to have benefits for patients, as well as cost-related outcomes. Clinical pharmacists will be shown to participate in the design and implementation of clinical drug treatment programs, as well as assisting clinicians in drug selection and rational drug use. As a result, it is demonstrated that patients no longer suffer from the same degree of drug-related problems, improving both the standard of clinical drug treatment today and the patients' quality of life.

Patients and Methods

Study Design

In this study, clinical pharmacists formulate management measures for Key Monitoring Drugs using evidence-based medicine and analyzing the DRPs of Key Monitoring Drugs over a period of five years, from 2015 to 2019.

Setting

The study is set in China at the Shandong Provincial Third Hospital (of the Cheeloo College of Medicine, Shandong University), a 1,400-bed tertiary university teaching hospital. In this setting, the costs and DRPs associated with Key Monitoring Drugs in the five years following their administration are investigated by a team of clinical pharmacists.

Establishing a Management Organization for the Study of Key Monitoring Drugs

The medical department and the pharmaceutical department jointly establish a working group for the supervision and management of the rational use of the drugs, while formulating measures for the management of their rational use in the hospital. The responsibilities of this working group include: dividing responsibilities between each department; determining the scope of the Key Monitoring Drugs to be included in the national advisory; and analyzing the dosages, statistics, and interventions that relate to DRPs. The key aim of the working group is to determine basic principles for the successful clinical application of Key Monitoring Drugs and to define the proper procedure for using these drugs according to evidence-based medical practice.

Determining the criteria for an evidence-based evaluation of the Key Monitoring Drugs

Regarding Key Monitoring Drugs, the administrative instructions provided by the manufacturer form the main standard for their evaluation. For medications without instructions, treatment guides for each specialized disease are referred to instead, and the PubMed database is searched for literature that supplies supporting evidence. Preliminary evaluations define the indication, dosage, solvent selection, course of treatment, contra-indications, and combinations that are suitable for each drug. Evaluation and classification of the quality of evidence are incorporated to establish criteria for the quality of evidence, so that the results of the study do not refer to unqualified documentary evidence. At present, the clinical studies that can be retrieved through the database mainly include randomized controlled trials, cohort studies, case-control studies, series case studies, case reports, traditional reviews, and expert opinions or experiences. The main widely-accepted evidence classification standards that are employed, meanwhile, are those of the evidence-based medicine center at Oxford University and the GRADE standard, which is formed from a combination of various classification standards; the resulting standards for evidence-based assessment are detailed in Table I[4,5].

Based on this work, a drug use "definition" for each Key Monitoring Drug is entered into the hospital's prescription system; a doctor can determine whether a Key Monitoring Drug is reasonable for medical application according to that definition[6-8]. The system then prompts the doctor to confirm "drug selection," "dose selection," "treatment duration," and so forth.

Types of DRPs, Their Causes Relating to Key Monitoring Drugs, and Clinical Pharmacists' Medication Interventions

DRPs are identified and properly managed by the clinical pharmacists who provide their recommendations to the healthcare team for each medication order. One measured outcome of this study is the number of pharmacists' interventions that are provided to manage DRPs that are encountered. The types of DRPs and their causes, as well as proposed interventions, are categorized according to the simplified form of the Pharmaceutical Care Network Europe drug-related problem classification (PCNE-DRP), version 9.0. For each event, two clinical pharmacists reach a consensus on a final decision that is based on the potential or actual clinical harm presented to the patient[9-11].

Comparative Analysis of Drug Cost

To evaluate the financial effects of intervention from clinical pharmacists, the costs of Key Monitoring Drugs (total cost, per capita drug cost, and proportion of Key Monitoring Drugs cost as part of the total drug cost) are statistically analyzed from 2015 to 2019; SPSS 21.0 software (IBM Corp., Armonk, NY, USA) is employed for single factor analysis[12,13]. Categorical variables are expressed as percentages, and continuous variables are expressed as means and standard deviations. Statistical significance is set at p-value < 0.05.

Results

Formulation of Clinical Application Principles for Key Monitoring Drugs

The management group shall integrate all expert opinions and discuss these with the pharmaceutical management professional committee to determine

Table I. Evaluation criteria.

Type of evidence	Evaluation essentials
Guide	It is essential to determine whether the literature has been reviewed comprehensively in the past.12 months and whether the supporting evidence for each recommendation has been marked with a level and a source. When determining the clinical application according to the level of recommendation: if a treatment is recommended as Class A then it can be used without contraindications; it can be used based on a Class B recommendation but it is noted that the evidence is not sufficient, or a decision as to whether or not it can be used can be based upon whether the evidence is sufficient. For Class B recommendations, it is important to pay attention to the publication of new evidence at all times. If treatment is recommended as Class C or D, this indicates that the evidence is lacking and there is great uncertainty; thus, the treatment drugs should be made unavailable.
Meta-review	It is essential to consider whether it is a systematic evaluation of randomized controlled trials; whether it has collected and included all relevant studies; whether it has evaluated the quality of a single trial; whether it has homogeneity among trials; whether it is meaningful, that is, how large and accurate the effect is; and whether the reliability and application value of its conclusions can be judged according to the evaluation of the authenticity and significance of the results of systematic evaluation.
Randomized controlled trial	It is essential that there is high-quality evidence. If there are limitations, inconsistent results, direct evidence is not provided, there are inaccurate results, or there are biased reports, then the quality of evidence will be decreased. The quality level of evidence will be improved if the observational study is designed rigorously, implemented well, found to be of significant efficacy, or there is a dose-response relationship.
Expert consensus	To determine whether expert opinions are reliable, is it essential to determine whether their opinions have sufficient basis in evidence. If there is no evidence, the expert consensus can be questioned. In the absence of research evidence, the consensus reached by multiple experts is relatively more reliable than that of individuals. For rare or complex conditions without research evidence, expert opinions have more important reference value.

Table II. Clinical application principles of key monitoring drugs.

Content	Specific requirement
Indication	It is forbidden to indicate that drugs may be used beyond the original drug specification, which medication shall be approved in strict accordance with. Any instances of approval of over-specification must be evaluated by evidence-based medicine and recorded in accordance with the relevant provisions for over-specification drug use. The compound preparation of two drugs can be carried out when the patient is suffering from two main diseases at the same time; otherwise, it should not be carried out.
Usage and dosage	Do not overdose. The single dose and daily dose shall not be higher than the recommended dose in the manual. Strictly follow the recommended administration frequency, solvent, and infusion concentration, as is specified in the instructions. Furthermore, do not exceed the course of treatment. Do not exceed the maximum number of days of treatment specified in the instructions. If a course of treatment is not prescribed in the instructions or evidence-base, it shall not exceed seven days.
Combined medication	Key Monitoring Drugs of the same type cannot be used in combination. Under non-special circumstances, each patient can only be prescribed with one type of Key Monitoring Drugs (classified by pharmacological action and indication, no matter whether administered orally or by injection). Special cases only include those where there are professional guidelines or there is authoritative evidence that recommends joint application.
Contraindication	Do not use contra-indications and do not use Key Monitoring Drugs that present risks.
Rational use of traditional Chinese medicine injection	Oral administered drugs are not suitable for injection and should be used in strict accordance with the functional indications specified in the drug manual. Traditional Chinese medicine used for promoting blood circulation and removing blood stasis has a wide range of pharmacological effects, but to avoid adverse drug reactions, it is stipulated that: those with a bleeding tendency shall not use this kind of medicine; this kind of medicine shall not be used in combination with non-steroidal anti-inflammatory drugs or platelet inhibition drugs. While mastering its modern pharmacological application, traditional Chinese medicine should be used according to symptoms differentiated by patients' tongue and pulse signs to play its best role and have the utmost effect; in this way, it is possible to combine traditional Chinese medicine and Western medicine in an appropriate manner.

the principles of clinical application for Key Monitoring Drugs[14]. The general principle is as follows: When Key Monitoring Drugs are used, the ratio of the drug cost versus curative effect should be fully considered, the least and the most economical drugs should be utilized to achieve the intended treatment purpose; special attention should be paid to the injection of traditional Chinese medicines (see Table II for specific clinical application principles).

Detailed Rules for the Use of the Definition of Key Drugs

The drugs in the list of Key Monitoring Drugs were defined one-by-one; the list has indicated supporting data and classifications for the drugs that go beyond their original instructions. Table III shows an example of drug definition for the Key Monitoring Drugs.

Drug-Related Problems

Descriptive statistics were calculated for variables relating to the types of identified DRPs and the medications associated with different types of DRPs[15,16]. The percentage error rate was determined by dividing the actual identified DRPs by the total number of reviewed drug prescriptions with potential DRPs. The types and causes of DRPs and clinical pharmacists' medication interventions can be seen in Table IV. The DRPs of Key Monitoring Drugs decreased by 45.50% from 2015 to 2019. The main DRPs were "Too many drugs prescribed for indication," "Inappropriate drug according to guidelines/formulary," and "Inappropriate combination of drugs". The incidence in which an intervention is proposed to a prescriber, the intervention acceptance rate, and the rate of solving problems have increased year on year. After an intervention is proposed to or discussed with the prescriber, the intervention is always accepted and either fully or partially implemented by the prescriber.

Effect Evaluation: Statistics of Drug Consumption Under Key Monitoring

To evaluate the overall effect, the consumption of Key Monitoring Drugs was assessed from multiple perspectives, including the total amount used, the

proportion of the income of Key Monitoring Drugs, and the cost of Key Monitoring Drugs per capita. In 2019, the total cost of the use of Key Monitoring Drugs decreased by 10.12 million CNY (Figure 1), in comparison to the cost in 2015.

In 2019, compared with 2015, the proportion of revenue gained from Key Monitoring Drugs (revenue from Key Monitoring Drugs/total drug use) decreased by 11.49% (Figure 2).

From 2015 to 2019, the per capita drug cost of Key Monitoring Drugs for in-patients gradually decreased and, in 2019, this resulted in a saving of 580.07 CNY per capita compared with the cost in 2015. The per capita cost of Key Monitoring Drugs for outpatients gradually decreased and, in 2019, this resulted in a saving of 74.61 CNY compared with the cost in 2015 (Figure 3).

SPSS 21.0 software (IBM Corp., Armonk, NY, USA) was employed for one-way ANOVA to assess the cost per capita of Key Monitoring Drugs for in-patients. The data include the costs per capita of Key Monitoring Drugs for in-patients over

Table III. Definition of key monitoring drugs.

Drug name	Indications and limitations	Contra-indication	Single maximum dose Maximum daily dose Maximum administration frequency Course of treatment Compatibility of solvents	Interactions and attention
Tanshinone II: a sodium sulphonate injection	Used for the auxiliary treatment of coronary heart disease, angina pectoris, and myocardial infarction.	Patients with a history of allergy to these drugs.	80 mg 80 mg 1 time only 7 days 5% glucose injection or 0.9% sodium chloride injection 250-500ml	Alprostadil can enhance the efficacy; cardiac function should be closely monitored when the two drugs are combined.
Troxerutin Cerebroprotein Hydrolysate Injection	Compound preparation of the two components should be selected when suffering from two main diseases at the same time, otherwise it should not be used as the first drug.	1. It is forbidden for use with patients with severe renal insufficiency. 2. It is forbidden for patients with an epileptic persistent state or grand mal.	10 ml 10 ml 1 time only 20 days 250-500 ml 0.9% sodium chloride injection or 5% glucose injection	It should not be used with balanced amino acid injection. Adverse interactions with antidepressants can lead to inappropriate stress. At this time, it is suggested to reduce the dosage of antidepressants [6].
Vinpocetine injection	To improve the symptoms induced by cerebral infarction, cerebral hemorrhage, and cerebral arteriosclerosis.	1. In the acute stage of intracranial hemorrhage, those who have not completely stopped bleeding after intracranial hemorrhage are forbidden from receiving this treatment. 2. Those who have serious ischemic heart disease and serious arrhythmia are forbidden from receiving this treatment.	30 mg 30 mg 1 time only Use no more than 14 days 5% glucose or 0.9% sodium chloride injection	When vinpocetine and methyldopa are used together, there is a slight synergistic effect on the latter, so it is advised that blood pressure is monitored when they are used together. Although there is no interaction between vinpocetine and drugs acting on nervous system, or antiarrhythmic and anticoagulant drugs at the same time in clinical research, it is still recommended to pay attention to observations when using vinpocetine in combination[7].

Table IV. Types and causes of drug-related problems and clinical pharmacists' medication interventions.

	Frequency (%)				
The cause	**2015**	**2016**	**2017**	**2018**	**2019**
C1 Drug selection					
C1.1 Inappropriate drug according to guidelines/formula	25 (12.5)	22 (11.64)	21 (12.21)	21 (12.88)	16 (14.68)
C1.2 Inappropriate drug (within guidelines but otherwise contra-indicated)	14 (7)	10 (5.29)	9 (5.23)	9 (5.52)	2 (1.83)
C1.3 No indication for drug	12 (6)	13 (6.88)	13 (7.56)	11 (6.75)	12 (11.01)
C1.4 Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	25 (12.5)	23 (12.17)	24 (13.95)	23 (14.11)	13 (11.93)
C1.7 Too many drugs prescribed for indication	35 (17.5)	27 (14.29)	22 (12.79)	23 (14.11)	12 (11.01)
C3 Dose selection					
C3.1 Drug dose too low	4 (2)	5 (2.65)	7 (4.07)	5 (3.07)	5 (4.59)
C3.2 Drug dose too high	22 (11)	17 (8.99)	19 (11.05)	16 (9.82)	9 (8.26)
C3.3 Dosage regimen not frequent enough	3 (1.5)	5 (2.65)	3 (1.74)	2 (1.23)	2 (1.83)
C3.4 Dosage regimen too frequent	20 (10)	21 (11.11)	17 (9.88)	15 (9.2)	9 (8.26)
C4 Treatment duration					
C4.1 Duration of treatment too short	10 (5)	13 (6.88)	7 (4.07)	6 (3.68)	6 (5.5)
C4.2 Duration of treatment too long	17 (8.5)	20 (10.58)	16 (9.3)	20 (12.27)	11 (10.09)
C9 Other					
C9.1 Inappropriate outcome monitoring (incl. TDM) or none	13 (6.5)	13 (6.88)	14 (8.14)	12 (7.36)	12 (11.01)
Total	200	189	172	163	109
Interventions					
I1 At prescriber level					
I1.1 Prescriber informed only	37 (18.5)	26 (13.76)	23 (13.37)	20 (12.27)	15 (13.76)
I1.2 Prescriber asked for information	37 (18.5)	30 (15.87)	22 (12.79)	19 (11.66)	12 (11.01)
I1.3 Intervention proposed to prescriber	72 (36)	85 (44.97)	89 (51.74)	95 (58.28)	64 (58.72)
I1.4 Intervention discussed with prescriber	54 (27)	48 (25.4)	38 (22.09)	29 (17.79)	18 (16.51)
I3 At drug level					
I3.1 Drug changed to	60 (30)	59 (31.22)	44 (25.58)	40 (24.54)	27 (24.77)
I3.2 Dosage changed to …	50 (25)	48 (25.4)	45 (26.16)	40 (24.54)	24 (22.02)
I3.3 Formulation changed to …	25 (12.5)	19 (10.05)	20 (11.63)	22 (13.5)	18 (16.51)
I3.4 Instructions for use changed to …	8 (4)	9 (4.76)	10 (5.81)	9 (5.52)	8 (7.34)
I3.5 Drug paused or stopped	27 (13.5)	29 (15.34)	28 (16.28)	28 (17.18)	17 (15.6)
I3.6 Drug started	30 (15)	24 (12.7)	25 (14.53)	24 (14.72)	15 (13.76)
Intervention Acceptance					
A1 Intervention accepted	147 (73.5)	151 (80.32)	143 (83.14)	138 (84.66)	97 (88.99)
A1.1 Intervention accepted and fully implemented	101 (50.5)	109 (57.67)	110 (63.95)	115 (70.55)	92 (84.4)
A1.2 Intervention accepted and partially implemented	28 (14)	30 (15.87)	20 (11.63)	13 (7.98)	2 (1.83)
A1.3Intervention accepted but not implemented	18 (9)	12 (6.35)	13 (7.56)	10 (6.13)	3 (2.75)
A2 Intervention not accepted	53 (26.5)	37 (19.68)	29 (16.86)	25 (15.34)	12 (11.01)
A2.1 Intervention not accepted: not feasible	23 (11.5)	24 (12.7)	23 (13.37)	21 (12.88)	8 (7.34)
A2.2 Intervention not accepted: no agreement	30 (15)	13 (6.88)	6 (3.49)	4 (2.45)	4 (3.67)
Status of the DRP					
O1 Problem solved	108 (54)	120 (63.49)	115 (66.86)	111 (68.1)	82 (75.23)
O2 Problem partially solved	21 (10.5)	19 (10.05)	15 (8.72)	17 (10.43)	12 (11.01)
O3 Problem not solved	71 (35.5)	49 (25.93)	42 (24.42)	35 (21.47)	15 (13.76)

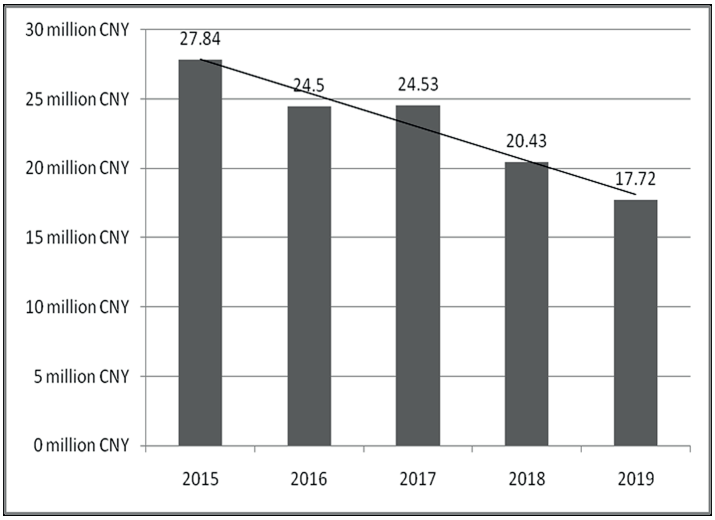

Figure 1. Changes in the total cost of Key Monitoring Drugs (CNY).

five years (2015-2019), which is expressed in the form of mean ± standard deviation ($x \pm s$). From the results in Figure 3, we see that the cost per capita of Key Monitoring Drugs for in-patients shows a downward trend for 2015-2019. Based on the one-way ANOVA results, the *p*-value is found to be less than the significance level of 0.01, which is statistically significant, indicating that the cost per capita of Key Monitoring Drugs for in-patients has decreased significantly over the past five years.

Discussion

To the best of our knowledge, this is the first prospective study describing the prevalence of drug-related problems in patients administered with Key Monitoring Drugs in mainland China. DRPs are commonly administered as a form of treatment in this patient population. This study's findings highlight the need for a clinical pharmacy service to support the use of Key Monitoring Drugs. The key causes of the DRPs identified were mainly the drug selection, dose selection, and treatment duration; this demonstrates the need for medication reconciliation by pharmacists. The interventions that were identified to succeed in rectifying DRPs mainly occurred at the prescriber level, when the prescriber was informed or asked for information, or when an intervention was proposed to or discussed with the prescriber. At a drug level, most DRPs were resolved when the drug was changed, the dosage

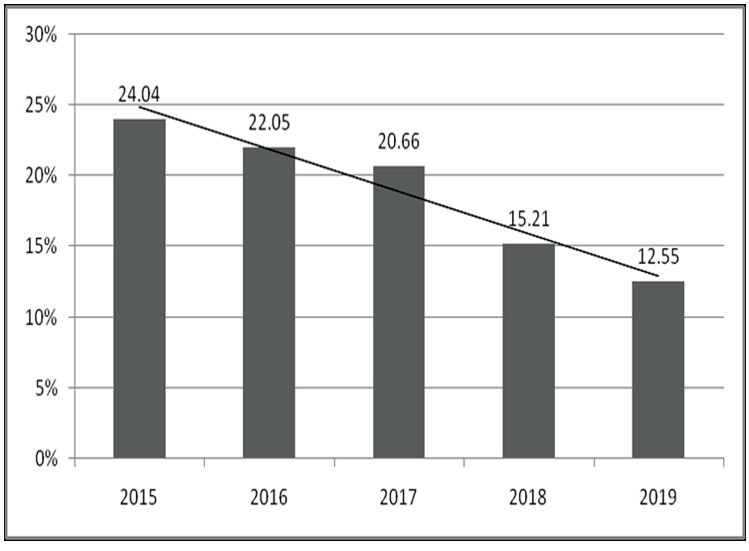

Figure 2. Changes in the proportion of the cost of Key Monitoring Drugs (%).

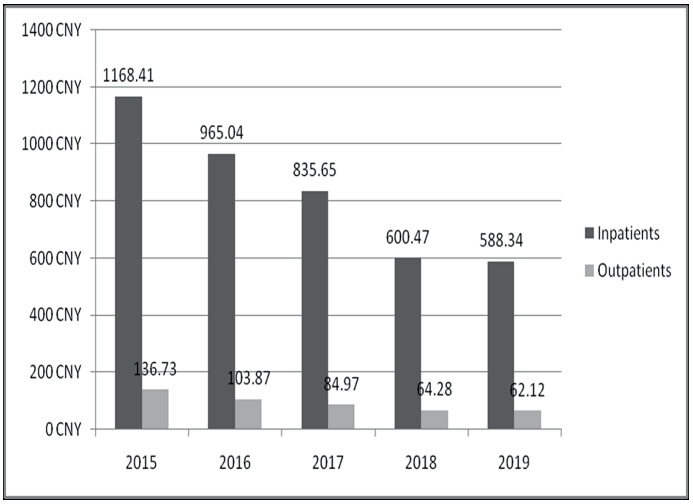

Figure 3. Changes in cost per capita of Key Monitoring Drugs (CNY).

was changed, or the drug was paused, stopped, or started. The intervention acceptance rate increased from 73.5% to 88.99%, and the rate of the problem being solved increased from 54% to 75.23%.

This study asserts that Evidence-Based Medicine should be fully relied upon in order to scientifically manage the administration of all drugs that meet the definition of Key Monitoring Drugs, in order to improve the safety of drug use, to put an end to the use of contra-indications, and to reduce the phenomenon of unreasonable drug use, such as over-indication. The exploration and formation of a Key Monitoring Drugs information management platform has been realized to improve work efficiency, coverage, and to form a new management mode. Meanwhile, the pharmaco-therapeutics and pharmaco-economics of the same kind of Key Monitoring Drugs with large dosages have been compared, so as to provide additional scientific references for clinical drug selection[17].

This study has focused on how to evaluate drug use scientifically and reasonably in the interest of the management of Key Monitoring Drugs. On one hand, the application of evidence-based medicine to evaluate the rationality of drug use can facilitate the development of cutting-edge, safe and rational drug use services for clinical purposes; this resolves the issues that the multiple drug delivery schemes face at present, which cannot be evaluated in terms of efficacy and economics. On the other hand, it can strengthen medical practice around Key Monitoring Drugs and improve the level of comprehension related to their use and the effectiveness of their management[18,19]. Finally, through the collection of drug efficacy cases for the purposes of economic comparison, if a scientific and orderly evaluation standard for the same types of drugs can be formed, then the selection of clinical drugs can be conducted in a manner that is more suitable with regards to clinical needs; gradually, this will achieve the ultimate goal of individualized drug use and refined drug treatment.

In April 2019, China's Health Commission issued a notice on drug use monitoring and clinical evaluation, which requires there to be a comprehensive evaluation of drug use and an application of the results in order to improve local medical support systems, clinical diagnoses, and the quality of treatment services. Key Monitoring Drugs are the agents that aid or increase the action of the principal drug, or that affect the absorption, mechanism of action, metabolism, or excretion of the primary drug (pharmacokinetics), in such a way as to enhance its effects. Key Monitoring Drugs are commonly used in the prevention or treatment of cancer, along with liver, cardiovascular, and cerebrovascular diseases. If Key Monitoring Drugs are properly administered, they can be beneficial for the recovery of patients from disease. Furthermore, they can shorten the period of hospitalization and reduce the cost of hospitalization so that the country's medical resources can be more effectively allocated. Conversely, Key Monitoring Drugs can increase the risk of a patient having an adverse drug reaction due to the increased use of combinations of drugs or the unnecessary use of drugs. Such adverse effects can prevent the patient's rehabilitation from the original

disease, prolong their length of stay in hospital, and increase the economic burden on patients and the healthcare system.

It has become a matter of public concern as to how to best strengthen the management of rational drug use and, thus, reduce the economic burden on patients. The management of adjuvant drugs has, in particular, become an important aspect of the management of rational drug use. The current excessive use of Key Monitoring Drugs not only leads to an increased incidence of adverse drug reactions and bodily damage, it can also increase the economic burden on patients and result in a wastage of medical resources. In 2017, the Chinese State Council issued a document on reforms and improvements that must be made to the existing policies relating to drug production and circulation. The document requires the use of antibiotics to be monitored, along with Key Monitoring Drugs and nutritional drugs, while irrational prescriptions are to be limited, and an interview system is to be established.

Conclusions

This is the first study to document clinical pharmacist-led interventions for identifying and solving DRPs related to the Key Monitoring Drugs. The impacts of the clinical pharmacists' long-term interventions on reducing the number of hospital re-admissions and generating financial savings have been evaluated compared with past studies[20-24]. The clinical use of Key Monitoring Drugs has been standardized by a scientific management system; this has been established based on the prescription review, administrative intervention, information management, and pharmaco-economic evaluation. The use of Key Monitoring Drugs in the hospital has now become increasingly standardized, the quality of drug treatment has improved, the proportion of Key Monitoring Drugs that are administered has decreased, and there has been a saving on unnecessary drug expenses for patients. This study has practical and effective reference value for the scientific management of Key Monitoring Drugs in other hospitals. The clinical pharmacists' recommendations, which are generally well-accepted by physicians, can assist with the prevention and alleviation of many DRPs along with their further complications.

Funding

Shandong Province 2019 TCM science and technology development plan project: Construction of TCM evaluation system based on real world evidence, decision tree and Markoff model (2019-0329); Key projects of China Pharmaceutical Association for promoting the dissemination of precision medicine science and technology (grant no. CMEI2019KPYJ(JZYY)00204)..

Authors' Contribution

Jing Yang, MD. Topic selection and manuscript writing. E-mail: yangjing201805@163.com; Lei Zheng, MM. Topic selection and financial support. E-mail: zhenglei8501@163.com; Wen-Gong Yu, MD (Corresponding Author). Manuscript writing and clinical pharmacist intervention statistics. E-mail: wengongyuouc@163.com; Yu-Chao Gu, MD (Corresponding Author). Manuscript writing and financial support. E-mail: guyuchao2021@163.com

Conflict of Interest

The Authors declare that they have no conflict of interests

References

1) U.S. National Library of Medicine. Adjuvants, pharmaceutic [EB/OL]. [2020-06-27]. https://www.ncbi.nlm.nih.gov/mesh/68000277.
2) Herxheimer A. Educating doctors to use drugs well [editorial]. Br J Clin Pharmacol 1976; 3: 111-112.
3) Han S, Zhong M T, Li J, Zhen J. The application status of Key Monitoring Drugs in our country and the management countermeasures study. Chin Pharm J 2016; 51: 96-100.
4) Steurer J, Roner S, Gnannt R, Hodler J. Quantitative radiologic criteria for the diagnosis of lumbar spinal stenosis: a systematic literature review. Bmc Musculoskelet Disord 2011; 12: 175.
5) Zhao H, Liu Y, Zeng J, Huang Y. Troxerutin cerebroprotein hydrolysate injection ameliorates neurovascular injury induced by traumatic brain injury--via endothelial nitric oxide synthase pathway regulation. Int J Neurosci 2018; 128: 1118-1127.
6) Yi Y, Zhang P, Wang R. Observation on the effect of Vinpocetine injection in treatment of the elder cerebral infarction. Chine J Modern Drug Appl 2013; 83: 327-331.
7) Moradi M, Mojtahedzadeh M, Mandegari A, Soltan-Sharifi MS, Najafi A, Khajavi MR, Hajibabayee M, Ghahremani MH. The role of glutathione-S-transferase polymorphisms on clinical outcome of ALI/ARDS patient treated with N-acetylcysteine. Respir Med 2009; 103: 434-441.
8) Neuroimmunology Group of Neuroimmunology Branch of Chinese Society of Immunology, Neuroimmunology Group of Neurology Branch of Chinese Medical Association, Neuroimmunology

Group of Neurology Professional Committee of Science and Technology, Committee of Chinese People's Liberation Army. Diagnosis and treatment guide of central nervous system tumor like demyelinating disease. Chin J Neuroimmunol Neuro 2017; 5: 23-90.

9) Jin H, Wang S, Hou L, Pan C, Li B, Wang H, Yu M, Lu Y. Clinical treatment of traumatic brain injury complicated by cranial nerve injury. Injury 2010; 41: 918-923.

10) Wu S, Sena E, Egan K, Macleod M, Mead G. Edaravone improves functional and structural outcomes in animal models of focal cerebral ischemia: A systematic review. Int J Stroke 2014; 9: 101-106.

11) Xiaochen W, Liqin Z, Chunge W, Qi D, Xin L. Systematic review of the efficacy and safety of gangliosides in preventing chemotherapy-induced peripheral neurotoxicity. Chin J Clin Pharmacol 2015; 24: 2462-2464.

12) Min LI, Tang Z Y, Shen X P. Efficacy and safety of low molecular weight heparin combined with edaravone in the treatment of progressive cerebral infarction: a systematic review. J Evid Based Med 2013; 13: 218-224.

13) Neural Injury and Repair Branch of Chinese Academy of Neuroscience. Expert Consensus on Neurological Damage and Repair of Brain Injury. Chin J Neurotrauma Surg (Electronic Edition) 2016; 2: 100-104.

14) Department of Neurological Injury, Traumatology Branch of Chinese Medical Association. Monosialic acid tetrahexose ganglioside sodium salt injection--expert consensus on treating patients with brain and spinal cord injury. Chin J Trauma 2010; 1: 6-8.

15) Gang SC, Xue ZY. Edaravone: good outcome as supplementary treatment for patients presenting with crescendo transient ischemic attack. J Chin Clin Med 2009; 4: 444-447.

16) Jin W, Lisheng Z, Li Y, Jun C, Shengfeng W, Jian Z, Shibing H, Zhengfeng F, Mingfeng W. Therapeutic effect of monosialic acid tetrahexose ganglioside sodium combined with edaravone on acute cerebral infarction. Evalu Analy Drug-Use Hosp China 2018; 169: 61¬-62.

17) Liao X, Zhang Y, Xie YM, Liu Y, Yi DH, Zhang YL, Chen F. Analysis of Diemailing Kudiezi injection use in real world in 7189 patients with cerebral infarction. China J Chinese Materia Medica 2016; 41: 4442-4450.

18) Yang J, Zheng L, Chen L, Song C. Establishment of clinical use management mode of adjuvant therapy drugs in our hospital. China Phar 2017; 28: 3545-3548.

19) Yang J, Zheng L, Guan Y, Song C. Analysis of the impact of antimicrobial management and rational use of antibiotics. Eur J Hosp Pharm 2020; 27: 286-291.

20) Qu C, Meng L, Wang N, Chen Y, Yang X, Wang J, Sun S, Qiu F. Identify and categorize drug-related problems in hospitalized surgical patients in China. Int J Clin Pharm 2019; 41: 13-17.

21) Zhu Y, Liu C, Zhang Y, Shi Q, Kong Y, Wang M, Xia X, Zhang F. Identification and resolution of drug-related problems in a tertiary hospital respiratory unit in China. Int J Clin Pharm 2019; 41: 1570-1577.

22) Ali MAS, Khedr EMH, Ahmed FAH, Mohamed NNE. Clinical pharmacist interventions in managing drug-related problems in hospitalized patients with neurological diseases. Int J Clin Pharm 2018; 40: 1257-1264.

23) Zheng Y, Li D, Zeng N, Guo H, Li H, Shen S. Trends of antihypertensive agents in patients with hypertension and coronary artery disease in a tertiary hospital of China. Int J Clin Pharm 2020; 42: 482-488.

24) Chen Q, Jin Z, Zhang P, Sun S, Li L, Liao Y. Characteristics of drug-related problems among hospitalized ischemic stroke patients in China. Int J Clin Pharm 2020; 42: 1237-1241.